Increased Gs Signaling in Osteoblasts Reduces Bone Marrow and Whole-Body Adiposity in Male Mice.

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Public Summary:
Bone is increasingly recognized as an organ that can regulate hormones and metabolism through secreting different factors. Although bone loss and increased body fat appear to be medically linked, it is unclear if increased bone formation can alter fat metabolism. We studied this by using an engineered protein to activate signaling in the bone cells of mice. We found that total body fat was significantly reduced starting at 3 weeks of age. The mice had significantly decreased serum triacylglycerides and increased sensitivity to insulin. The mice showed resistance to fat accumulation from a high-fat diet. These findings suggest that immature bone cells can influence fat metabolism in conditions of increased bone formation and suggest a role for their use in the regulation of whole-body fat and metabolic maintenance.

Scientific Abstract:
Bone is increasingly recognized as an endocrine organ that can regulate systemic hormones and metabolism through secreted factors. Although bone loss and increased adiposity appear to be linked clinically, whether conditions of increased bone formation can also change systemic metabolism remains unclear. In this study, we examined how increased osteogenesis affects metabolism by using an engineered G protein-coupled receptor, Rs1, to activate Gs signaling in osteoblastic cells in Col1(2.3)(+)/Rs1(+) transgenic mice. We previously showed that these mice have dramatically increased bone formation resembling fibrous dysplasia of the bone. We found that total body fat was significantly reduced starting at 3 weeks of age. Furthermore, Col1(2.3)(+)/Rs1(+) mice showed reduced O2 consumption and respiratory quotient measures without effects on food intake and energy expenditure. The mice had significantly decreased serum triacylglycerides, leptin, and adiponectin. Resting glucose and insulin levels were unchanged; however, glucose and insulin tolerance tests revealed increased sensitivity to insulin. The mice showed resistance to fat accumulation from a high-fat diet. Furthermore, Col1(2.3)(+)/Rs1(+) mouse bones had dramatically reduced mature adipocyte differentiation, increased Wingless/Int-1 (Wnt) signaling, and higher osteoblastic glucose utilization than controls. These findings suggest that osteoblasts can influence both local and peripheral adiposity in conditions of increased bone formation and suggest a role for osteoblasts in the regulation of whole-body adiposity and metabolic homeostasis.